

U.S.S.N. 09/821,203

Filed: March 29, 2001

AMENDMENT AND RESPONSE TO OFFICE ACTION

In the Claims

1-20 (canceled)

21. (currently amended) An improved method of detecting changes in the expression of genes in a microarray, wherein the genes comprise an E-box regulatory sequence, or encode proteins or cofactors that bind to the E-box regulatory sequence, the improvement comprising

a) providing a set of primers for reacting with a nucleic acid sequence in the genes in the microarray, with the sequences having a length of between 480 and 700 base pairs and a melting point of between 75 and 85°C, and comprising a non-consensus sequence so that there is no detectable hybridization with homologous sequences;

b) reacting the set of primers with the genes to amplify the nucleic acid sequence to form amplicons;

c) arraying the amplicons produced for the reaction in step (b) onto a solid support; and

d) reacting the amplicons with a labeled probe comprising all or a portion of the non-consensus sequence; and

e) detecting levels of hybridization between the amplicons and the labeled probe, thereby detecting levels of gene expression; and comparing the gene expression to the expression of control genes, thereby detecting any changes in expression levels.

22. (currently amended) The method of claim 21 for screening for differential expression of one or more E-box regulatory genes or genes interacting with genes binding to the E-box regulatory sequence, comprising:

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- a) providing a first library of genes associated with a particular disease, disorder or state,
 - b) providing a second library of genes, obtained from cells having a different state, disease, or disorder ~~or expressed~~ to a compound to be tested,
 - c) detecting or measuring expression of selected genes in the first and second library using the method of claim 21,
 - d) comparing the expression of the selected genes in the first and second libraries, and
 - e) detecting which genes have altered expression in the second library.
23. (previously presented) The method of claim 22 wherein the state is selected from the group consisting of age, cancer and diseases or disorders of the cardiovascular, neurological, and musculoskeletal systems.
24. (original) The method of claim 22 wherein the compound is a drug or toxin
25. (previously presented) The method of claim 22 further comprising normalizing results of expression by comparison with levels of expression of housekeeping genes.
26. (currently amended) The method of claim 21 for determining the effect of a compound on the disease or state of an individual comprising:
- a) providing a DNA library, including ~~one or more E-box regulatory genes~~ comprising an E-box regulatory sequence or encoding proteins or cofactors that bind genes that interacting with genes binding to the E-box regulatory sequence, wherein the genes are obtained from the

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individual after treatment of the individual, or cells or tissues derived therefrom, with to the compound or a particular dosage regime of the compound,

b) screening the library for changes in levels of expression of the selected genes using the method of claim 21, and

c) correlating the changes in expression with the state, disease or disorder prior to treatment.

27. (original) The method of claim 26 wherein the cells or tissues are treated with one or more compounds *in vitro* prior to making the DNA library.

28. (currently amended) The method of claim 26 wherein the compound is selected ~~from~~ from group consisting of proteins or peptides, sugars or polysaccharides, nucleic acid molecules, and synthetic molecules.

29. (original) The method of claim 26 wherein the library is derived from cells obtained from an individual of a particular age, having a particular disease or disorder, or derived from the neurological system, the cardiovascular system, the musculoskeletal system, or cancerous tissues.